The Canadian Medical Association Journal

Vol. I.

JANUARY, 1911

No. 1

THE ANCIENT FOUNDATIONS OF HEREDITY

By A. B. Macallum, Ph.D., Sc.D., F.R.S.

Professor of Biochemistry, University of Toronto

IN selecting as the subject of my address the ancient foundations of heredity I have been influenced by a desire to use the opportunity to help in clarifying ideas about a matter which is not too clearly understood.

About six months ago a paper was published by Professor Karl Pearson and Miss Elderton upon the effect of the alcohol habit in heredity; and it was pointed out that the statistics available showed that alcohol used in excess by one generation does not necessarily result in deterioration of the next or a more remote generation. This conclusion was much criticised, and it was held that the evidence on which it was based was too slender, or of too narrow a scope, to support such a startling view. With this criticism it is possible to agree; but not a few of the critics assumed that heredity is, at foundation, a function which can be affected by adventitious influences and that, therefore, immediately acquired vicious habits in the matter of food and drink indulged in by the people of one generation seriously affect the physique and psychological character of their offspring, immediate or remote. According to this view such agents as alcohol and tobacco, when used to excess, directly influence heredity and result in physical and moral degeneration.

Now, there is no doubt that degeneracy is to a certain degree associated with alcoholism. It is also a fact that the nations of civilization, without an intention to that end, are making a gigantic experiment in regard to the effect of alcohol on the race, the result of which will not be determined in this or in many generations from now. There is,

Opening address of the Medical Faculty of the University of Liverpool, October 4th, 1910.

further, no reason to question the opinion that degeneration, formerly subject to the law of the survival of the fittest, is now on the increase in the denser centres of population, and it is disquieting to learn that the one-quarter of this nation which produces one-half of the children contains the vast majority of the degenerate class

It is, however, well to ascertain the true bearings of all these facts on each other before we associate any, or all, of them in the relation of cause and effect; for it is only through a right appreciation of the forces involved in bringing about the disquieting results that we can succeed in discovering an effective remedy.

Now, it is not at all likely that the biologist and the physiologist will confuse the situation. They, from their studies of animal and vegetable forms, recognize that heredity is a force which is affected by external, physical or chemical conditions, only after these have acted on the organisms for a long period of time, and that to the steady, stable character of this force is due the more or less pronounced fixity of type in species, genera, and races in the animal and vegetable kingdoms. There is a school, it is true, which maintains, as its cardinal doctrine, that heredity is not necessarily a stable and certain force, and that through this instability new species may suddenly arise, and facts are adduced which apparently support this opinion. But this school numbers only a few disciples, and the influence on biological thought which it exerts is correspondingly limited. The doctrine of heredity as an invariable force dominates in biological philosophy.

This doctrine is not an ancient one. Forty years ago it was practically unknown. Darwin in his "Theory of Pangenesis," advanced in 1873, appears to have accepted the view that external conditions directly affect the germ plasm of a species. It was only in the early "eighties" that Weismann disposed of this view, and established the immutability of the germinal material, except in a manner that is in no way due to the action of external forces. Although his doctrine has been keenly criticised, and although he has, as a result of the demonstration of weak points in it, modified somewhat its rigidity, it is accepted by the great majority of biologists.

This doctrine is not yet thirty years old, and in consequence it is not surprising that it has not yet made its way into the general thought of to-day. It is, indeed, not adequately grasped by the world of science itself, for one finds here and there evidence of a tacit recognition of the view that the germ plasm can be affected in a single generation by external conditions. An example of this is found in a recent contribution of Oscar Hertwig in which he appears to accept the unscientifically determined view of specialists in neurological medicine, that chronic

alcoholism in an individual does alter the heredity-bearing properties of his germ plasm.

It is of the greatest importance that right views should prevail amongst non-scientific thinkers and critics regarding the principles of heredity, for it is only in this way that they may be fully prepared to face the problems which profoundly affect racial welfare. There can be no remedy, except an empirical one, against disease, unless we know the causation of disease; and this knowledge can only be obtained after the principles which determine, or control, the normal condition have been ascertained. Racial degeneration is a disease, and its control, or cure, therefore, demands, primarily, a thorough understanding of the forces that contribute to, or are responsible for, the normal conditions. Those, therefore, who are students of social and economic conditions and of the effects of these in promoting racial degeneration must, first of all, thoroughly comprehend the stability of the force of heredity, if the results of their efforts are to be of service in checking one of the greatest dangers to civilization.

In consequence of these considerations, I have thought it advisable to draw attention to the question on this occasion and to put in a more or less succinct way the salient aspects of the great law of heredity. To do this without going over some familiar ground is of course not possible; but it seemed to me that the question might have a new interest if it were treated from an unusual point of view. That fresh point of view may be found in the study of how heredity arose and how it has been maintained throughout all the history of life on this earth. This comprehends all that is involved in the ancient foundations of heredity, and it is this which shall be my theme during the remainder of this address.

The duration of life has been variously estimated from twenty million years up to a thousand million years. The tendency, as our knowledge widens, has been to postulate a longer and longer period, and to-day those who have given attention to the subject hesitate rather at the acceptance of a short period than at the assumption of a long one. This would make one hundred millions of years a conservative estimate. If we accept this as safe, we may still regard it as a sweep of time of enormous length in which many things could have happened to influence in a remarkable degree the course of the history of living material. What living organisms are to-day is the result of all the forces which acted for a century of millions of years at least.

In this enormously long period changes were brought about in the structure and character of the cell, which constituted valuable adaptations to its environment and developed the function of heredity. What these were are of moment, for they throw a clarifying light on the forces that have made for heredity. Those changes are, however, only to be comprehended through a careful study of all the types of animal and vegetable cells. This includes not only the structure, but also the chemistry and physics of the cell, and it is, therefore, necessary, before developing this theme, to review a few of the leading facts bearing on the structure of the cell as it is to-day.

The cell, the smallest unit of life, is formed of what is known as protoplasm. This consists of different kinds of proteins, and these are the most complicated compounds known. Protoplasm in its typical state is capable of growth, repair, and all the other activities and manifestations characteristic of living matter. This and its peculiar chemical and physical constitution, which it is endowed with the power to control, make it a unique phenomenon in the world of matter. Indeed, its very life is dependent on its power to maintain a large measure of independence of the world without itself.

Assisting in the maintenance of this individuality, and enclosing the whole mass, there is at least one membrane which differs in character in different cells. In the vegetable cell there may be two such membranes, one external, usually very thick and consisting of cellulose or allied carbohydrate material, the other very delicate, almost imperceptible and immediately limiting the protoplasm from which it differs in composition slightly but differs in properties in a very marked degree. This is the only membrane in animal cells as a rule, and in both animal and vegetable cells it is endowed with special properties. Through one of these the membrane is impermeable, to a certain degree, to salts or inorganic elements present in the surrounding fluid; because of this the cell is in great measure protected against its environment. It is also because of this impermeability that the cell retains in its interior not only its own proteins but also its own dissolved and digested food stuffs. The membrane, owing to this property of impermeability, has played an enormous part in the life of cellular organisms in the struggle for existence.

Situated more or less centrally in the protoplasm which constitutes the bulk of the cell, there is what is called a nucleus. This is a more or less spherical body which is enclosed by a membrane of its own, whose properties I shall discuss later. The material included in the nucleus is chiefly formed of a substance known to the biologist and cytologist as chromatin, to the chemist as nucleo-protein. The name chromatin was given to this substance because of the property it possesses of absorbing the staining matters or dyes used in the preparation of cellular material for microscopic examination. A nucleo-protein, on

the other hand, is formed of a protein and a remarkable combination of phosphoric acid united with bodies, known as purins and pyrimidins, through sugar molecules acting as connecting links.

As the bio-chemist prepares this nucleo-protein it is comparatively simple, but we must not conclude that it represents wholly the chromatin of the histologist. In the method of preparation of nucleo-protein the chromatin must undergo very considerable changes, and the nucleo-protein thus obtained can only be held to represent in a general way the original material, and no more, in fact, than the skeleton of the verte-brate, freed from all the soft attached parts, represents the living animal. The chromatin of the cytologist must, accordingly, be regarded as an exceedingly complicated compound, perhaps much more complicated than any other compound found in the living cell, and to this must be due the extraordinary rôle that chromatin plays in the life of the cell.

The evidence which recent studies on the cell have furnished has on the whole indicated that this chromatin is not formed in the nucleus but in the cytoplasm, that is, in the protoplasm outside of the nucleus. The latter is, therefore, a storehouse for the chromatin as soon as it is formed, for only in rare instances is chromatin ever found in detectable quantities outside of the nucleus. This is an important point to remember in the effort to understand the rôle the nucleus plays in cell life and in heredity.

When the cell has attained a certain size and its nucleus contains a correspondingly increased quantity of chromatin, both undergo division into two new cells, each with its own nucleus. In this the original nucleus manifests changes in its structure and appearance, changes which are grouped under the term mitosis, derived from the Greek word μίτος a thread, and so named because the chromatin in the early stage of nuclear division is gathered in the form of extended loops of thread ranged parallel to each under the membrane and between two opposite poles, like the lines of longitude on a globe representing our planet. These loops then divide in the line of the equator, the membrane now disappears, the U-shaped parts, called chromosomes, resulting from the division of the loops, are transported to the equatorial plane, and there. or even before, each splits longitudinally, giving rise to two apparently equal daughter chromosomes. These latter are then borne to a point beyond the two poles of the original nucleus. Not only is there an equal number of chromosomes at each pole, but of every two chromosomes resulting from the longitudinal splitting of each original chromosome. one goes to each pole, which becomes the centre for a new nucleus. The chromosomes then lose their individual character and fuse in such a way that they ultimately give a mass of vesiculated chromatin like that usually prevalent in the ordinary nucleus. This mass becomes enveloped in a new membrane, and then the cell body itself divides, giving two daughter cells each with its nucleus.

Now there are many points and exceptions in the process of division which I have not touched on. I have simply dwelt on those which are essential to the development of my subject on this occasion. I would direct attention specially to the chromatin and its history in the nucleus, to the properties of the nuclear membrane, and to the functions of the delicate cell membrane to which I have already referred.

From all the observations which have been made on the chromatin and the chromosome, and on their history and function, there can be no doubt of their vast importance in the life of the cell. The chromatin inside the nucleus guides the life of the cell and even makes its continuance possible. Gruber has shown that if unicellular organisms, such as infusoriæ, are divided by the knife, only those parts survive and reproduce themselves, which contain at least a portion of the nucleus. Parts which contain no trace of a nucleus may survive for a few hours, but they ultimately disintegrate. This makes it quite clear that the chromatin, the essential part of the nucleus, is of supreme importance to the life of the cell. How it affects this is at present unknown, but although it is a product of the action of the cytoplasm outside the nucleus. it may in turn give off continuously a substance or substances which act as stimulants or hormones, inciting and developing the synthetic or anabolic processes of the cell, as a consequence of which the cell is active and assimilative. This, I think, is the only explanation of the rôle that the nucleus plays in maintaining the continuity of the life of the cell.

Then there is the rôle of heredity. In this the chromatin plays the only part. It is now established, as a result of years of observation on the fertilization of ova in animals, that the essential element transferred from the male to the female cell is chromatin. In the transformation of the male cells into spermatozoa the chromatin is enclosed almost alone in the head, which is but a modified nucleus, and when this penetrates the ovum its chromatin goes to unite with a portion of the chromatin of the ovum to form a new nucleus which starts the development of the ovum. The new organism thus arising manifests in its development the characters of both parents. The chromatin transferred through the head of the spermatozoon to the ovum carries to the latter the qualities of the male parent. Boveri succeeded in fertilizing the ovum of an echinoderm, which had been deprived of

its nucleus, with the spermatic element from another species. The cell body of the new organism thus came from the female parent, the chromatin of the nucleus from the male. The characters which the new organism presented on development were those of the species to which the male parent belonged. This fact and that already mentioned, namely, that in fertilization as ordinarily observed the only material transferred from the male to the female cell is chromatin, make it abundantly manifest that the chromatin is the heredity-controlling substance.

It would appear that it is the chromatin which determines the sex of the offspring. McClung discovered that in certain insects there are two kinds of spermatozoa differing chiefly in the quantity of chromatin in the head. Fertilization with the spermatozoa of one kind, he was inclined to believe, gave rise to males only, while fertilization with the other gave female offspring only. These observations have been confirmed by the investigations of others. In certain of the arachnids and myriapods two kinds of spermatozoa are also present. More recently, also, Boveri and Gulick determined that in the nematode worm, Heterakis, there are also two kinds of spermatozoa. one of which furnishes to the impregnated ovum five chromosomes. the other, four. The developed ovum resulting from fertilization with the spermatozoon yielding four chromosomes is always male, that due to fertilization with the other is always female.

One might multiply instances to prove that the chromatin is the substance in the sexual cells which determines the character of the offspring. What I have advanced here will suffice to show also that the chromatin directs the life of the cell and is responsible for all its specific manifestations.

One can attribute the different manifestations to differences in composition in the chromatin of different kinds of cells. There is no escape from this conclusion. Five years ago Bardeen exposed the fresh spermatozoa of a toad to the action of x-rays for a period of from ten to thirty minutes and found that the longer exposure killed the organisms, while the shorter so affected them that, when they were used to fertilize ova from the same species, the larvæ developing from these were found to lack one cerebral lobe, one lung, one kidney, or some other structure of the normal form. More recently, Oscar Hertwig, by exposing echinoderm sperm and ova, and also the sperm and ova of frogs, to the action of radium for a time, obtained results which are almost as striking. The spermatozoa after a certain length of exposure were not killed. Indeed, in all such cases, they manifested as vigorous and active a movement as those which had not been subjected to the

action of radium, and yet, when these were employed to fertilize normal ova, larvæ did not develop, or, if development took place, it progressed only to an early stage in which the larvæ were found to exhibit either defect of structure or a great want of vitality. In the frog larvæ so produced both kinds of phenomena were observed in the same examples. Echinoderm larvæ which reached the pluteus stage were inactive on the floor of the aquarium, while the normally produced larvæ swam freely and vigorously in the upper layers of the water.

The explanation for all this is not far to seek. The chromatin owes its heredity-controlling property to its own chemical constitution, which, as already pointed out, must be exceedingly complicated, so much so that millions of isomers of it, differing only very slightly from each other, may be present in the same nucleus or spermatic head. It is, it must also be held, the number and character of these differences that determine the inheritance of parental characters by the offspring. The molecules, simply because they are complicated, are less stable than if they were simple in constitution, and on this account are easily affected by emanations from radium or by rays from the cathode terminal, just as sensitive salts of silver in the photographic plate are affected by light. Changes, great or small, in the constitution of the molecules result, and, in consequence, there may be a failure of development or, if larvæ are obtained, they exhibit more or less profound defects of structure.

It is manifest, then, that heredity, as a controlling force in the maintenance of a type and in the transmission from generation to generation of special characters and qualities, is in the last resort dependent on the complex chemical constitution of the molecules of chromatin. being so it may be asked how it falls out that with so labile an element as chromatin there is so little change in its molecules under ordinary conditions. The answer to this question is that the physical and chemical constitution of the cell, as well as its structure, is of such a character as to reduce the possibility of such a change to a minimum. Changes do occur, however, which no structural, physical, or other constitution of the call can prevent; for a complex, chromatin molecule may alter in composition simply from its own complexity and unwieldiness just as a huge and complicated house of cards may collapse in whole or part more readily than a simpler one. It is, indeed, to such spontaneous changes in the chromatin of the germ cells that we must attribute the variations which a species may exhibit.

In order to understand how the physical and structural characters of the cell reduce the tendency of the chromatin to vary, it is necessary to consider here the properties of the membrane surrounding the nucleus. It has been found, as a result of a large number of observations, that the normal nucleus contains no carbohydrates or fats, and that, besides chromatin, there is present a simpler protein which serves as a stroma or framework for the nuclear cavity. There are, further, in the normal nucleus, no inorganic salts, either free, combined, or absorbed, it matters not how abundant these may be in the cytoplasm without the nucleus.

We have, then, in the nucleus a structure that does not know the inorganic world and whose contents consist of a complicated nucleo-protein derived from cytoplasm, where it is produced, and of a protein which may possibly also be of external origin. This, associated with the fact that all the chromatin in a cell is usually contained in the nucleus, is significant. Outside of the nucleus all is activity, synthesis, and change. Within there is stability and uniformity in all but the amount of the chromatin, for this is ever varying with the cyclic activity of the cell. The nucleus is the storehouse for the cell, holding and protecting its contents from changes which would be inevitable if there were free communication between the cytoplasm and nucleus.

This protective action is the property of the nuclear membrane. It allows the passage in either direction of chromatin, but of nothing else. During the life of the cell, except for the short period when nuclear division is proceeding, this membrane persists and performs its functions in this way. The nuclear membrane, then, is a structure, one of whose functions is to protect the heredity-controlling substance from change. The composition of this membrane is not in all species of cells the same. The nuclear membrane of the hepatic cell is not exactly the same as that of a pancreatic cell or of a germ cell, and it is perhaps because of this that the chromatin contained in a hepatic nucleus is different from that which is found in the nucleus of a pancreatic cell. species of nuclear membrane allows only chromatin of a certain type, out of all that may diffuse about it, to pass within. In consequence, a liver cell, however it may develop and divide, gives rise only to other liver cells; a pancreatic cell, only to pancreatic cells, and an embryonic germ cell, only to germ cells. We may suppose that the nuclear membranes of the germ cells act as a filter for the chromatin of a germinal type, which may be formed in all parts of the body; for it is difficult to believe that the germ cells which are affected in their nutrition by the body tissues and fluids do not receive from the other cells contributions of their chromatin. Whether the nuclear membrane may allow such chromatin to enter will doubtless depend on the character of the membrane. A slight alteration in that character should permit of variations in the offspring.

In Darwin's theory of pangenesis the body gives off from all its parts gemmules which, collected in the germ cells, reproduce in the offspring the characters of the parents, whether of inherited or immediately acquired origin. A germ cell, according to this theory, is but a microcosm of the individual organism producing it. The theory was advanced to explain not only heredity but what was accepted almost universally forty years ago; namely, the transmission from parents to offspring of such alterations in characters as mutilations may effect. The possibility of such transmission is now accepted by very few thinkers. and in consequence the theory has been abandoned on all sides, while Weismann's doctrine of the continuity of the germ plasm has taken its place. According to this the substance in the germ cells, which serves as the basis of heredity, is handed down from generation to generation unaffected by the history of the individual parental organisms, but subject to an inherent tendency to develop differences of composition within narrow limits, which on accumulation in a species would account for the formation of new characters. According to Weismann, the germ cells, though forming part of the body, never receive any material from the latter that influence their subsequent history, while the theory of pangenesis postulates that the material in the germ cells which determine the character of the offspring is derived from all parts of the parental organism. Put thus,—for the last twentyseven years they have been so contrasted,—the two theories are mutually exclusive. On the explanation which I have given of the origin of the germinal chromatin and its filtration by the nuclear membrane, are these theories so opposed and mutually contradictory? Does it not appear more rational to regard the truth as divided between them?

I must, however, leave the theoretic side of this question and pass on to what is of immediate moment.

The nuclear membrane then has functions of extraordinary significance in the life of the cell. Further, mitosis, or the process of nuclear division, is indispensable to heredity, for a cellular organism that would not make equal division of its chromatin between its daughter cells could not endow both of them with its own characters. One of the two might receive all or the greater part of the chromatin, in which case the other, lacking in some of the heredity-controlling substance, would be a degenerate and be exterminated in the struggle for existence. Division in such a case would be merely a waste of material, not an effort at reproduction. The processes of mitosis and the physical properties of the nuclear membrane are consequently of vast importance in heredity; and in order to give due emphasis to this importance I now propose to show that these foundations of heredity are of extremely ancient origin.

All life on the earth to-day originated from an organism at the beginning in the far past. How that organism itself originated we do not know. Whatever its origin, it was probably ultra-microscopic and became of microscopic size only after a long period of time. It did not then have a nucleus and the chromatin it formed was probably more or less diffused throughout its mass. Division occurred, but heredity was not developed, and only became so when in the struggle amongst a multitude of organisms whatever was of value in that struggle could be transmitted to the offspring in a species. The sexual process also had not developed. Even to-day such non-nucleated organisms as the Cyandphyceæ, the blue-green algæ, are wholly asexual in all their cycles of life. The first development must have been a mechanism by which the cell, when it divided, gave to each of the two new cells not only half of the whole cytoplasm but also, and more important, one-half, or approximately one-half, of the whole of its chromatin. this purpose, perhaps, besides mitosis, which is now the dominant method, other methods were evolved. One of them still persists in the foraminifer Calcituba polymorpha. In this form the nuclei are without a membrane, and it forms only when about to divide. This results in the production not of two but of ten daughter nuclei by a process which is utterly unlike mitosis. If we read the history of this form backwards, we will recognize that the nucleus was in all cases first without a membrane.

That mitosis only gradually developed would seem to be indicated by the defects that we still see in some primitive forms. In Peridineæ we find it does not go beyond the first stage. These, which are the chief phosphorescent forms in the ocean, are amongst the oldest types of living matter persisting to-day, and are probably direct descendants of the forms which existed before there was any specialization into animal and vegetable organisms. Of a similar origin is *Euglena* in which a defective mitosis is found.

In the end the process, that of mitosis, which gave almost or complete equality in the shares of the chromatin between the two daughter nuclei, was evolved. This occurred before the uncellular organisms became distinctly animal and vegetable in their characters, for the mitosis of the vegetable cell is in all points essentially the same as that of the animal cell and, consequently, there must have been a common origin for both. About the same time the nuclear membrane began to be a persistent organ.

The development of this structure may have been furthered by the growing salinity of the sea water. When vertebrates first made their appearance the salts in the sea were probably in concentration not more than one-third what they are now, and this date was far on in the history of life on the earth. It is probable that the earliest ocean water was merely faintly salt, but by the time the primal cell had reached the stage in which the nucleus made its appearance the saline concentration had increased, the salts were influencing the vitality and heredity of the organisms, and, in consequence, a membrane unpermeable to salts and protecting the heredity-controlling substance from change became of enormous value, and was evolved.

It would seem that the sexual process in its essential features made its appearance first at this same stage. It also is practically the same in vegetable as in animal cells, and hence its common origin. The very fact that only organisms, vegetable as well as animal, which are nucleated undergo the sexual process shows that the latter is of very ancient origin.

All this development, therefore, happened far, far back in the history of the earth, and long before multicellular organisms arose. The rocks which are grouped under the general name Huronian are the most ancient in geological history, and yet in the upper divisions of this period, that is in what is called the Pre-Cambrian, there are found remains of highly developed animal forms. Animal and vegetable cells must have attained their typical characters ages before that. The foundations of heredity were, therefore, laid in the very earliest stage of the earth's history.

How long ago that was one cannot say. As I have already stated, one hundred million years is a conservative estimate of the time during which life has existed on the globe. Joly's estimate of the age of the earth, based on the amount of sodium chloride now in the ocean and the amount annually discharged into it by the rivers, approximated ninety millions of years. That, as Dubois has pointed out, is probably much under the mark, but even this leaves the imagination in despair. We may, however, say that for scores of millions of years the organs of heredity in the cell have been performing their function. They are consequently not greatly less ancient than life itself.

Because of the steady action of these same organs, life has been handed down through the long ages. Is it surprising, in view of all this, that they should to-day, as they will in the far future, act as unerringly as unfalteringly as in the remote past? These foundations, laid so long ago, are primal, and their dislocation for a single generation would bring the history of life on earth to an abrupt end.

To suppose, therefore, that any external condition, any food-stuff or alcohol, acting for one or many generations, can affect the hereditycontrolling chromatin, is to underestimate the forces that have played their part in the cell for scores of millions of years. For ages the physical conditions in the environment of living matter have been trying and testing those very forces and their foundations, only in the end to make them firmer and firmer as time passed. Is it reasonable to believe that any external agency or condition, such as our artificial modern life provides, can in a century or two undo all that has been so slowly and laboriously established in the long past?

And yet some one may ask: Is alcoholism not closely associated with degeneracy? To that I would answer: Yes, but as a symptom or a result, and not a cause, of degeneracy. I hold that to regard it as a cause of degeneracy is about as futile as to claim that intellectual deficiency is the cause of the defectively developed brain.

Nor can racial degeneration be brought about by underfeeding any more than by overfeeding. You will hear it not infrequently stated that the economic conditions of our modern civilization are responsible for the degeneracy of type which may be found in the slum districts of densely populated cities, and that if economic conditions were improved not only would misery and poverty disappear, but degeneracy would be eliminated from the race. Misery and poverty may be alleviated in this way, but to hope that degeneracy would thus vanish is to indulge in a foolish dream. Can the economist, the philanthropist, or the statesman, or all three combined, add by thinking on their behalf one cubit to the intellectual stature of a family of mental degenerates? In the words of Sidney Smith, "You might as well try to poultice away the humps of a camel."

The error on this point has arisen from confusion of ideas. Underfeeding, overcrowding, and other unhygienic conditions do affect the physique of the individual in a marked degree, and if he is subject to such conditions during the years of his development he reaches maturity more or less stunted and with correspondingly deficient physical, and perhaps also mental, powers. He in popular estimation would be classed as a degenerate. His children brought up under the same conditions and with the same results are similarly classed. If now their children are reared under healthier conditions and with a sufficiency of food they may-I do not say they will-be normal in physique and mentally vigor-Here it would consequently appear to follow that the improvement in the surroundings and a sufficiency of food have eliminated degeneracy from a stirps, but the mistake made is to suppose that the individual of the first instance or the children of the next generation were degenerates. They are no more examples of degeneration than are individuals who are afflicted with chronic tuberculosis.

Genuine degeneracy is more fundamental than this. Sufficiency of food and improved hygienic conditions can no more counteract it

than they can convert a member of the black race into a white man. It is the heredity-controlling chromatin that is at fault in degeneracy, and this result is an effect of the tendency to spontaneous change in the chromatin. This tendency is responsible for more than this, for it is the factor in the production of new and unusual characters distinctive of what, in biological language, are called "sports." A newly developed character of this type may not represent a desired improvement, but the reverse and the individual in which it appears may thus be far below the type from which it arose. On the other hand, the sport may represent a greatly improved variety, and thus be a progressive form while the other would be a degenerate. So in the human species the alteration of the germ chromatin due to this tendency to spontaneous change may result in the production of a degenerate or of an individual of much more than average capacity.

This variability of the germinal chromatin is, as I have already pointed out, of two sources. In one case, the altered chromatin may be derived from without, through a slight alteration in the nuclear membrane permitting it to diffuse through into the nuclear cavity. In the other case, it arises from the labile character of huge molecules which are apt of themselves to disintegrate or change in their constitution ever so slightly, and consequently minute changes may occur early in the chromatin of the sexual cells.

These two kinds of variability are such that no structure or organdetermining heredity could prevent. It is well, however, that it is so; for if variability were excluded there would be no progress. The first unicellular organisms, if endowed with rigidly and unerringly working functions of heredity, would never have given rise to higher and more complicated types, and to-day after millions of years the only life on our globe would be that of some one simple protobiont form. There is in variability, therefore, a factor which has made for evolutional progress. The organs of heredity have safeguarded what of value has been won, and have excluded change due to the action of external forces. The only variations which occur are those which no arrangement of a structural, physical, or chemical character could prevent.

On this view, degeneracy of type must be regarded as always dogging the heels of evolutional progress, but it has never hitherto retarded it, for the conditions of existence which have prevailed in the past have eliminated the unfit. In the human species also these same conditions, combined with disease, have operated in the past in the same way. To-day the spirit of humanity, aided by science, has largely checked the operation of these factors, and the result is likely to be of the gravest import to the race. What effective remedy for this there may be, I do

not know. That suggested by Sir Francis Galton can only be palliative. A religion that has as one of its special tenets the restriction of the reproduction of the unfit may have its effect eventually. In the eleventh and twelfth centuries the monasteries of Europe were filled from the ranks of the ablest and best of the race, and this, in Hallam's opinion, lowered the average mental capacity of the later Middle Ages and led to a prolongation of the barbarism of the earlier. It may, in the future, be possible to use the force of religion to segregate, not the best, but the unfit, in celibate communities, and thus raise the average mental capacity of the race. At present, however, this would appear only to be a dream.

Though we may not hope for the present, we need not despair for the future. To take the first step towards a solution of a problem, we must diagnose accurately the cause of the morbid condition. To do that we must also recognize what a force heredity is, of how ancient an origin it must be, and how it may, if at all, be influenced. To know, and recognize clearly, these things will at least save time and prevent the application of quack remedies to a situation the right treatment of which will always call for the most expert knowledge and the exercise of the most thoughtful foresight of the state. Therein lies the high duty of physiology to humanity.